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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,639	06/26/2001	Randolph J. Noelle	P 0280639	9079

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	6

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/888639	Applicant(s) NOELLE
	Examiner GAMBEL	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 4/1/02

2a)☐ This action is FINAL. 2b)☑ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 1-50

4a) Of the above claim(s) _____ is/are withdrawn from consideration. 22-23, 36-37

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 1-21, 24-35, 38-50

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☑ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☑ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. Upon a review of the instant claims, it has been determined that the numbering of claims is not accordance with 37 C.F.R. 1.126. The original numbering of the claims must be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When claims are added, except when presented in accordance with 37 CFR 1.121(b), they must be renumbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not). There is no original claim 39 in the instant application.

Misnumbered claims 40-51 have been renumbered 39-50.

The dependency of the renumbered claims 39-50 have been amended to recite the appropriate claim(s).

Applicant's election of the species anti-gp39 antibodies is acknowledged.

Applicant's request that the non-elected gp39 species be rejoined with the elected species, as the search required for both species would be substantially co-extensive.

As pointed out in the last Office Action, anti-gp39 antibodies and soluble CD40 are distinct species because their structures and modes of action are different. Therefore, claims 22-23 and 36-37 have been withdrawn from consideration as being drawn to the non-elected species.

Claims 1-21, 24-35 and 38-50 are under consideration in the instant application.

2. Formal drawings, filed 6/26/01, comply with 37 CFR 1.84.

3. No Information Disclosure Statement has been filed with the instant application.

4. Applicant should amend the first line of the specification to update the status of the priority documents.

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

6. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 6, 19, 33, and 43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

It is apparent that the MR1 antibody / hybridoma is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the pertinent cell line / hybridoma which produces this antibody. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

8. This is a rejection under 35 USC § 112, first paragraph, "written description" (and not new matter).

Claims 1, 2, 9-15, 24-30, 38-42 and 48-50 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

There is insufficient written description encompassing any "antagonist of the receptor on the surface of the T cell which inhibits the interaction of the ligand with the receptor" or "a gp39 antagonist" other than targeting gp39 / CD40 ligand with anti-gp39 / CD40 ligand antibody (or the other gp39 Antagonists set forth on page 5, paragraph 3 of the specification) because the relevant identifying characteristics such as structure or other physical and/or chemical characteristics of said "antagonists" as well as the "receptor on a surface of a T cell which mediates contact dependent helper effector function" are not disclosed.

Applicant is relying upon certain biological activities and the disclosure of a particular receptor on a helper T cell" (i.e. gp39 or CD40 ligand) as well as certain known antagonists of CD40 ligand-mediated interactions (e.g., anti-CD40 ligand antibody, soluble CD40 /CD40lg) as limited representative species of to support an entire genus of receptors on T cells as well as antagonists. The instant invention encompasses any antagonist or T cell receptor that results in the desired binding and inhibitory effect, yet the instant specification does not provide sufficient written description as to the structural features of said antagonists and receptor that would provide a correlation between the chemical structure and the desired binding and inhibitory function.

The reliance on the disclosed gp39 / CD40 ligand and the known CD40 ligand antagonists of anti-CD40 ligand antibodies and soluble CD40 does not support the written description of any "antagonist" or "receptor on a T cell". It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biological or pharmacological activities. Structurally unrelated binding antagonists encompassed by the claimed "antagonists" would be expected to have greater differences in their activities. Further, the structure and mode of action of the CD40 ligand differs from other known and unknown T cell receptors that mediate contact helper dependent effector functions.

Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.
Thus, the specification fails to describe these DNA sequences. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicant has not provided sufficient written description of any "antagonist of the receptor on the surface of the T cell which inhibits the interaction of the ligand with the receptor" or "a gp39 antagonist".

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

In the absence of structural characteristics that are shared by members of the genus of "antagonist of the receptor on the surface of the T cell which inhibits the interaction of the ligand with the receptor" or "a gp39 antagonist" ; one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

9. Claims 1, 2, 9-15, 24-30, 38-42 and 48-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of anti-gp39 / anti-CD40 ligand antibodies (and soluble CD40), which is not under consideration' see above), does not reasonably provide enablement for the use of any "antagonist of the receptor on the surface of the T cell which inhibits the interaction of the ligand with the receptor" or "a gp39 antagonist" in the claimed methods to induce T cell tolerance or specific non-responsiveness.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to use the invention commensurate in scope with these claims.

There is insufficient disclosure does not enable any "antagonist of the receptor on the surface of the T cell which inhibits the interaction of the ligand with the receptor" or "a gp39 antagonist" because there is insufficient direction and guidance as to the relevant identifying characteristics such as structure or other physical and/or chemical characteristics of said "antagonists" or "T cell receptors" capable of inducing T cell tolerance or specific non-responsiveness. Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies or enables any "antagonists" or "T cell receptor".

It is not sufficient to define a specificity by an ill-defined functional property or ambiguous structural properties. Also, an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property, that is, an "antagonist of the receptor on the surface of the T cell which inhibits the interaction of the ligand with the receptor" or "a gp39 antagonist" for methods of inducing T cell tolerance or specific unresponsiveness.

Therefore, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use of the claimed "gp39 antagonist" or "antagonist of a receptor on a surface of a T cell which mediates contact dependent helper effector functions" to target any "receptor on a surface of a T cell which mediates contact dependent helper effector functions" in order to induce T cell tolerance or specific unresponsiveness, commensurate in scope with the claimed invention.

Applicant is relying upon certain biological activities and the disclosure of a particular receptor on a helper T cell" (i.e. gp39 or CD40 ligand) as well as certain known antagonists of CD40 ligand-mediated interactions (e.g., anti-CD40 ligand antibody, soluble CD40 /CD40lg) as limited representative species of to support an entire genus of receptors on T cells as well as antagonists. The instant invention encompasses any antagonist or T cell receptor that results in the desired binding and inhibitory effect, yet the instant specification does not provide sufficient enablement as to the structural features of said antagonists and receptor that would provide a correlation between the chemical structure and the desired binding and inhibitory function in order to make and use antagonists of T cell receptors to treat autoimmune diseases commensurate in scope with the claimed invention.

The reliance on the disclosed gp39 / CD40 ligand and the known CD40 ligand antagonists of anti-CD40 ligand antibodies and soluble CD40 would not lead the skilled artisan to predict how to make and use any "antagonist" to target any "receptor on a T cell" to induce T cell tolerance or specific unresponsivness, commensurate in scope with the claimed invention. It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biological or pharmacological activities. Structurally unrelated binding antagonists encompassed by the claimed "antagonists" would be expected to have greater differences in their activities. Further, the structure and mode of action of the CD40 ligand differs from other known and unknown T cell receptors that mediate contact helper dependent effector functions.

For example, since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function.

The success of state of the art structure-based strategies for inhibitor design is highly unpredictable. For example, Kuntz (Science 257:1078-1082, 1992) on page 1080, column 3, discloses that as little as 2% of compounds predicted to inhibit specific enzymatic or receptor systems actually show inhibition in the micromolar range. Kuntz further discloses that "optimization" of these compounds has proven even more problematic. Therefore, in view of the unpredictability in the art, and in view of the insufficient guidance and working examples in the specification, the quantity of experimentation required by one skilled in the art to practice the invention undue.

Without such guidance, making and using the claimed "antagonist(s)" to target any "receptor(s)on a T cell" to induce T cell tolerance or specific unresponsiveness would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. See In re Fisher, 166 USPQ 19 24 (CCPA 1970).

10. Claims 1-21, 24-35 and 38-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

Applicant has not disclosed how to use gp39-specific antagonists in combination with antigen-presenting cells (APC) to induce antigen-specific T cell tolerance therapeutically for the antigens and species encompassed by the claimed methods. There is insufficient information or nexus with respect to the in vivo ability of gp39-specific antagonists and APC to accomplish the claimed therapeutic endpoint of immunological tolerance.

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the therapeutic indices of biopharmaceutical drugs and particularly tolerance induction can be species- and model-dependent, it is not clear that reliance on the limited in vivo experimental models accurately reflects the relative efficacy of the claimed tolerance induction regimens.

In agreement with the art-known experience; Noelle et al. (U.S. Patent No. 5,876,718) discloses that anti-gp39 may have different effects being used and the method of presentation (see column 24, lines 3-5). Although gp39-specific antibodies have been able to induce some immunosuppression in certain murine strain combinations, it is not clear that a state of immunological tolerance has been achieved or simply immunosuppression. More importantly, it is not clear that the skilled artisan would extrapolate the ability to induce immunological tolerance from these limited murine experimental results to the breadth of targeted antigens including alloantigens encompassed by the claimed invention.

It is not clear that the instant murine experimental transplantation systems provide the strong histocompatibility antigenic barriers associated with the therapeutic targets encompassed by the claimed therapeutic strategies for inducing tolerance (rather than immunosuppression). A problem with murine systems is the ease with rejection can be suppressed.

Tolerance is the long-lasting nonreactivity of the immune system to a specific set for antigens, maintained without on-going immunosuppression. Many different strategies have been developed to achieve transplantation tolerance some have which led to indefinite graft survival in rodents, none of these strategies have yet been applied to human patients in a way that allows reliable withdrawal or exogenous immunosuppression. Auchincloss (chapter 11 in Transplantation Immunology, Bach and Auchincloss Eds. Wiley-Liss, New York, 1995, pages 211-218, see page 211). While tolerance inducing strategies that have worked well in rodents, such strategies have been much less successful even when tested in nonhuman primates and other large animals. Also, the Conclusion on page 217 states that Although more than a dozen different techniques to induce tolerance in rodents are now available, the fact remains that none of them has been used successfully in the clinic. Inducing transplantation tolerance in human must therefore be very hard to do. And that reading of this chapter should be wary of simple solution to this complex approaches

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective tolerance-induction therapies, undue experimentation would be required to practice the claimed therapeutic in vivo methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed in vivo methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for inducing antigen-specific T cell tolerance.

11. Claims 6, 19, 33, and 43 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6, 19, 33 and 43 are indefinite in the recitation of "MR1" because its characteristics are not known. The use of "MR1" antibody as the sole means of identifying the claimed antibody (and hybridoma) renders the claim indefinite because "MR1" is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation to define completely distinct hybridomas / cell lines .

Amending the claim to recite the HB11048 hybridoma deposited with the ATCC would obviated this rejection.

The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1-21, 24-35 and 38-50 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lederman et al. (U.S. Patent No. 6,403,091) in view of Berschorner (U.S. Patent No. 5,597,563) and Cobbold et al. (U.S. Patent No. 6,056,956).

Lederman et al. teach the use of 5C8-specific / CD40L-specific antibodies, including chimeric and humanized antibodies (see columns 7-8) to inhibit the immune response, including methods of inhibiting the rejection of transplanted tissues, including heart, kidney and liver (see column 11, paragraph 6) as well as to treat diabetes (see column 11, paragraph 7) (see entire document).

Lederman et al. differs from the claimed invention by not disclosing the use of an additional allogeneic or xenogeneic cell in transplanting tissues and organs of interest.

It is noted that the allogeneic or xenogeneic cells employed in the instant methods are an additional element(s) with respect to the transplanted tissue or organ per se. For example, transplanted tissues and/or organs, including the bone marrow would comprise allogeneic or xenogeneic cells; but these types of transplanted tissues and organs do not appear to be the substance of the instant claimed methods.

Berschorner teach methods of inducing antigen-specific immune tolerance by providing antigen presenting cells containing the antigen to which specific tolerance is desired (see entire document, including Background of the Invention, including column 2, paragraph 2, Detailed Description of the Invention). Berschorner also teach that the antigen presenting cells, which can be isolated from a number of hemopoietic tissues and can include dendritic cells, Langerhans cells and mononuclear phagocytes (e.g., see column 6, paragraphs 3-4) would be administered with an immunosuppressant agent contemporaneously with the antigen presenting cells (see Detailed Description of the Invention, including column 8, column 4). Both alloantigens and xenoantigens are targeted (see columns 5, paragraph 4 - column 6, paragraph 1), including the treatment of a number of diseases (see column 6, paragraph 2).

Cobbold et al. teach methods of preventing graft rejection in tissue and organ transplants with anti-T cell antibodies in order to induce tolerance by providing antigen (see entire document, including columns 1-4). Cobbold et al. teach the provision of the antigen and the immunosuppressant at different times to provide an tolerance-permissive environment (see column 1-4).

Given the teachings of providing antigen and/or antigen presenting cells containing the antigen to which specific tolerance is desired, including those at the time transplant, contemporaneously with immunosuppressants, as taught by Berschorner and/or Cobbold; one of ordinary skill in the art would have been motivated to combine the immunosuppressive properties of the CD40L-specific antibodies, taught by Lederman et al., to create an environment conducive to tolerance or specific unresponsiveness in the transplantation of a number of tissues and organs at the time the invention was made.

Given the teachings of Cobbold et al. that the presence of antigen as well as the use of anti-T cell antibodies can provide an environment conducive to tolerance or specific unresponsiveness, one of ordinary skill in the art would have had a reasonable expectation of success and motivation to employ the CD40L-specific antibodies in combining antigen presenting cells in transplanting a variety of tissues and organs at the time the invention was made.

Given the prior art teachings of inducing nonresponsiveness to both alloantigens and xenoantigens as well as the use of a variety of antigen presenting cells to a variety of transplanted tissues and organs, one of ordinary skill in the art would have employed a variety of antigen presenting cells, including those encompassed by claims 9-11, 24-26, 38-40, and 48-50 as known antigen presenting cells, particularly the ready availability of human B cells as antigen presenting cells at the time the invention was made. Also, transplanting a number of tissues and cells, including those encompassed by 13-14 and 28-29 was known and practiced by the ordinary artisan at the time the invention was made.

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Berschorner AND/OR Cobbold et al. to those of Lederman et al. to provide methods of providing an environment conducive to tolerance or specific unresponsiveness by combining an immunosuppressant such as the CD40L-specific antibodies, taught by Lederman et al. With a source of alloantigen or xenoantigen, as taught by Berschorner and Cobbold et al. To transplant a variety of tissues and cells. A person of ordinary skill in the art would have been motivated to produce this resultant therapeutic regimen to provide an environment conducive to tolerance or specific unresponsiveness to decrease the rejection of the transplanted tissue or organ and to increase the survival of such transplants. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-21, 24-35 and 38-50 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over
claims 1-34 of U.S. Patent No. 5,683,693,
claims 1-34 of U.S. Patent No. 5,902,585, and
claims 1-7 of U.S. Patent No. 6,375,950

Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending claims and the patented claims appear to read on the same or nearly the same methods of inducing specific unresponsiveness. Further, the patented claims appear to anticipate the instant methods.

16. Claims 1-21, 24-35 and 38-50 are directed to an invention not patentably distinct from claims 1-34 of commonly assigned U.S. Patent No. 5,683,693 and claims 1-34 of commonly assigned U.S. Patent No. 5,902,585 for the reasons set forth above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Patent No. 5,683,693 and U.S. Patent No. 5,902,585, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

17. No claim allowed.

The method claims drawn to the use of the MR1 antibody appear to be free of the prior art. It appears that the MR1 bind the mouse CD40L and the 5C8 antibody binds the human CD40L.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
January 13, 2003

John J. Doll, Director
Technology Center 1600